cell adhesion molecule-1 (VCAM-1), alpha-1 acid glycoprotein (AGP) and C-reactive Protein (CPR) for two homozygous sickle cell patients, and it's association with clinical episodes, hemoglobin S% determination and donor cell percentages. We report two patients with Sickle cell disease (SCD) had multiple Cerebro-Vascular-Accident (CVA) and recurrent vasco-occulsive crises and failed to respond to chronic transfusion program with Desferal rescue, underwent HLA-matched Allogenic Bone Marrow Transplantation (BMT). Patients were prepared for transplantation using standard regimen which comprised Busulfan (BU) 3.5 mg/kg PO every 6H for total of 16 doses, four days of Cytoxan (50 mg/kg) and, ATG (30mg/kg) for 3days. Both were given antiseizure prophylaxis from day-2 to day +14 and continued with cyclosporin (1.5 mg/kg) for 6 months post-transplant and because of poor renal function patient #1 received methylprednisone 1mg/kg as alternative to methetotrexate while patient #2 received standard short course of methetrexate for GVHD prophylaxis. Neutrophil Engraftment (0.5× 109/L) occurred in day+10, day+14 respectively with augmentation of GCSF. Both had stable clinical and cytogentic engraftment. Post BMT complication were significant for SVS (superior vena cava syndrome) which completely resolved with r TPA for patient #1 and chronic cutenous GVHD for patient #2 which managed with steroid. Pre BMT adhesion molecules VCAM-1, AGP and plasma factor CRP were determined and correlated with clinical episodes of crises, Hgb S% and donor cell percentage. VCAM-1 level was 1041 ng/ml, AGP 1.14 mg/L, and CRP 11.64 mg/L on day −4 for patient #1 which declined by 38% on day +16 for VCAM-1 16%, and 100% for AGP and CRP respectively. While VCAM-1 level was 3404 ng/ml, AGP 1.14 mg/L, and CRP 11.64 mg/L for patient #2 on day-2, these were noticed to decline gradually and reach minimum of 970 ng/ml (down by 71%) of VCAM-1, 1.0 mg/L of AGP (12%), and almost 100% decrease of CRP. Our results suggest the role of Stem cell allograft in reversing the progression of vasculopathy through decreasing adherence and interaction of both red cell, endothelial cell and plasma factors.

Table.

	VCAM ng/mL (#1)	AGP mg/L (#1)	CRP mg/L (#1)	VCAM ng/mL (#2)	AGP mg/L (#2)	CRP mg/L (#2)
Post BMT	871	0.948	0	970	1.0	0

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THE USE OF FLUDARABINE BASED REDUCED INTENSITY CONDITIONING FOR THE TREATMENT OF PATIENTS WITH FANCONI'S ANEMIA

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Allogeneic stem cell transplantation (SCT) is the only curative modality for Fanconi's anemia (FA). FA patients are most susceptible to alkylating agents and radiation at dose ranges commonly used in preparation for SCT. For FA, fludarabine based non-myeloablative stem cell transplantation (NST) is particularly attractive for reducing toxicity and improving immediate and long-term outcome following SCT. Sixteen FA patients were transplanted in our center between 1989-2002. Eight patients were transplanted with cyclophosphamide and ionizing irradiation (total lymphoid irradiation) (CY-TLI). Six patients were treated, with NST consisting of fludarabine 30mg/meter sq/day × 6; cyclophosphamide 5mg/kg/day ×2 and rabbit anti-T lymphocyte globulin (ATG) 10mg/kg ×4. Higher dose of cyclophosphamide of 10mg/kg/day ×2 was used in a patient with leukemic transformation with thrombocytopenia and 20% myeloblasts. The regimen was well tolerated with no transplant related toxicity or any major complication. However, rejection was observed when the protocol was applied for a matched unrelated donor (MUD). A second transplant from another unrelated donor was successfully accomplished without complications using a combination of fludarabine, busulfan 4mg/kg/day ×2 and Campath-1H (humanized anti-CD52), and therefore, it was decided that this protocol will also be used for a subsequent case. All 8/8 patients treated with NST with stem cells obtained from a matched sibling or MUD survive, following uneventful SCT procedure with 100% donor cell chimerism, fully reconstituted with no severe acute or chronic GVHD, whereas in the CY-TLI group 50% are currently alive post transplantation. Moreover, looking at several parameters associated with post-transplant complications, like fever, infections, the need for total parental nutrition, veno-occlusive disease of the liver and graft-versus-host disease, NST protocol appears superior according to all parameters. Based on our data, fludarabine based NST may represent the treatment of choice for patients with FA with a matched sibling or MUD available.

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REDUCED INTENSITY (RI) CONDITIONING AND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN PEDIATRIC PATIENTS WITH NON-MALIGNANT DISORDERS

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Because children tolerate intensive regimens with less TRM, there has been reluctance to use RI regimens in them despite potential benefit for reduced long-term morbidity. RI regimens are of interest in children with nonmalignant disorders since there's no obvious need for high-dose therapy or GVL. Of 30 pts who underwent RI HSCT at Children's Memorial Hospital, 12 (6M, 6F) had nonmalignant disorders. Diagnoses: 5 immunodeficiencies (2 Hyper-IgM, 1 Omenn's, 1 X-linked lymphoproliferative disease, 1 chronic granulomatous disease), 3 metabolic disorders (1 Hurler's, 1 mucolipidosis II/III, 1 Sandhoff), 4 hemoglobinopathies (3 sickle cell, 1 beta-thalassemia). Median age: 6 yrs (range 0.5-22.5). Stem cell sources: PBSC from 6 unrelated donors, 4 matched siblings, 1 mismatched parent, and 1 unrelated cord blood. Regimen: fludarabine 30 mg/m^2 (day (d) −10 to −5), IV busulfan, 0.8-1 mg/kg×8 doses or 3.2 mg/kg ×2 doses (d −5 and −4), and equine ATG 40 mg/kg or rabbit ATG 2 mg/kg (d −4 to −1). GVHD prophylaxis: CsA (7), CsA/MMF (5). Median time to ANC >500/ul = 19 d (10-61), and to unsupported platelet count > 20,000/ul = 16.5 d (10-61). Median time to full donor chimerism (VNTR 95-100%) = 143 d (14-473) in 8 of 11 evaluable pts (1 hyper-IgM pt remains a mixed chimera, 2 with hemoglobinopathies never developed donor chimerism). One hemoglobinopathy pt achieved full donor chimerism but rejected at 2 yrs (after PBSC boost). Post-HSCT PBSC boosts were given to 5 pts for falling donor chimerism. One pt developed aGVHD II-IV; 3 of 8 surviving past d100 with donor chimerism developed limited (2) or extensive (1) cGVHD. Median survival is 609 d (7-1251). Of 12 pts, 8 are alive. 100d TRM occurred in 2 (measles encephalitis in 1, ARDS in Omenn's pt who began conditioning with active infection/ARDS and died d+7). Six of the survivors continue to show donor chimerism. The 2 survivors with autologous recovery are hemoglobinopathy pts. Whereas 1 of 4 hemoglobinopathy pts had sustained engraftment, 7 of the 7 remaining evaluable pts have stable engraftment. Immunodeficiency pts had obvious clinical benefit from HSCT but more time is needed to assess impact of RI HSCT in pts with metabolic disorders. In children with nonmalignant disorders other than hemoglobinopathies, this RI regimen is relatively non-toxic and promotes engraftment, even with unrelated donors. However, in children with hemoglobinopathies, this RI regimen is associated with non-engraftment or late graft rejection and should not be performed.

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A TEST DOSE OF I.V. BUSULFAN (BU) IS PREDICTIVE OF THE AREA UNDER THE CURVE (AUC) OF A SINGLE DAILY DOSE OF I.V. BU IN PEDIATRIC PATIENTS UNDERGOING A REDUCED INTENSITY (RI) HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT)

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High-dose BU-containing chemotherapy has been used in autologous and allogeneic HSCT. Variations in the PK for oral BU in pediatric patients have resulted in either decreased effect or increased toxicity. The IV formulation eliminates the variability of